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LASERS

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INTRODUCTION

The optical laser was first developed in 1960. Among the first medical applications for lasers was the dermatologic application of this Ruby laser in 1964. Since that time, the application of lasers in medical and surgical uses has grown quite extensively. Within the field of otolaryngology, Jako began his pioneering work in 1967 with the use of the Carbon Dioxide laser for laryngeal applications. Also in 1967, Sataloff reported the first applications of Neodymium and Ruby lasers for otosclerosis. The acceptance of lasers within the field of otolaryngology has progressed to the point now, that the American Board of Otolaryngology recommends that each residency program provide residents with experience and instruction in safety and use of, at a minimum, the Carbon Dioxide laser. The list of types of lasers in routine use within the field of Otolaryngology-Head and Neck Surgery is growing daily with a partial list that includes the Carbon Dioxide, Argon, ND:YAG, KTP and Flash Lamp or Argon Pumped Dye Lasers. Experimental lasers which have not yet received FDA approval for otolaryngology applications, but which may hold potential for the future include the Excimer lasers and other near and mid infrared laser such as the Erbium YAG and Holmium YAG. One of the future lasers under development as an off-shoot of the strategic defense initiative is the Tunable Free Electron Laser. This laser, although still experimental, eventually has the potential for being tunable from X-ray wavelengths to far infrared, and provide

power levels ranging from milliwatts to megawatts. This laser may eventually be the ultimate answer to the question of (Which laser, When and Why?)

Vital to understanding the current and future laser instruments and applications is an understanding of three principle parameters of laser energy: wavelength, power density, and timing. In addition, its also necessary to have an understanding of the interaction of these three parameters with biological tissue to fully appreciate the range of biological effects that result.

This chapter is a brief introduction to laser biophysics. This will include the generation of the laser beam, the transmission of the laser beam to the tissue, and the understanding of some of the limitations. In addition, this chapter will introduce the concept of optical biophysics i.e. an introduction to the interaction of light with tissue and the resulting biological effects.

HISTORY

The ideological basis for the concept of the laser was proposed in the late 19th Century with atomic Quantum Theory. Einstein in 1917 predicted the existence of a phenomenon known as the stimulated emission of energy from atoms. This was only a theory until Schawloss and Towns in 1958 developed the first working maser (microwave application by stimulated emission of radiation). They were awarded the Nobel Prize for this. (Chester

Gould) The maser operating in the microwave length was invisible. The first visible laser (Light Application by Stimulated emission of Radiation) was invented in 1960 by Maiman. Advances came quickly with the development of the gas laser in 1961 by Javan, the Neodymium Glass Pulse laser by Johnson in 1961 and the CO_2 laser by Patel in 1964. The Ruby laser invented by Maymen in 1960 was first applied for medical applications by Leon Goldman in the field of dermatology for the treatment of port-wine stains with moderate success. Sataloff in 1967 reported the effects of Neodymium Glass lasers and Ruby lasers used for stapedotomy and otosclerosis with some success. Since that time, the introduction of the Argon laser, Neodymium YAG laser, KTP laser, Argon Pump Dye and Flash Lamp Pump Dye have all been shown to have unique and beneficial applications within the field of medicine and surgery.

The future history of laser development applications looks very bright. In the near future, head and neck applications of the Excimer (near ultraviolet) and newer infrared lasers such as the Erbium YAG (2.9 micron wavelength) and Holmium YAG (2.12) show great promise.

Within the field of otology, the CO_2 laser, KTP and Argon laser have been the lasers most studied and used. Each laser has some distinct advantages based on understanding of their wavelength/tissue effects and each in turn has several distinct disadvantages which will be covered more in depth in the section on laser tissue interaction.

BASIC LASER PHYSICS

In this section, we will explain the generation of the laser beam itself, and include some description of the various laser systems relating to the types of lasers and the delivery systems that are unique for each laser.

GENERATION OF A LASER BEAM

The basic phenomenon of lasing takes place usually at the atomic level, although certain lasers such as the Argon laser use ions, and the Carbon Dioxide laser uses molecules. For purposes of the initial discussion here, we will discuss the generation of a laser beam from a single atom. The atom is generally represented as a core of neutrons and protons surrounded by a cloud of electrons located in discrete orbitals. Those orbitals that are more distant from the nucleus contain electrons of higher energies. These energies are directly related to the distance from the nucleus. In the early 19th Century, the atomic Quantum Theory proposed that each of these discrete orbitals are separate and independent. This implied that there was not a continuous gradation of energies between orbitals and that a unique energy was necessary to change the electron from one orbital to another orbital. The most stable configuration of an atom is called the ground state. This state represents the lowest possible energy present within that particular atom.

When atoms absorb energy, these electrons are elevated to

higher energy levels. An excited electron may spontaneously

this energy and decay back to a lower orbit (lower energy

state). This energy released must correspond by the laws of

conservation of energy to the energy that was originally placed

into the system to excite this electron to a higher energy level

in the first place. This energy may be released as a photon (as

light) and/or as heat, (as kinetic energy). This release of

energy may occur in several transitions or in one large

transition. The spontaneous release of energy if it is omitted

as light, is called spontaneous emission. Molecular lasing

differs somewhat from atomic lasing in that molecules are much

more complex structures. Not only do molecules have unique

electron orbitals as earlier stated, but they also have

rotational and vibrational modes that may also represent higher

energy states. As molecules increases in size or the number of

atoms, the potential number of energy levels increases. Large

organic molecules that form the substrate for lasing in an Argon

Pumped Dye laser thus can be responsible for a broad range of

output wavelengths.

Stimulated emission of energy was proposed by Einstein in

1917, as was predicted from Quantum Theory. Energy transitions

must be initiated by input of energy of the appropriate discrete

amounts. A photon entering the system of appropriate energy level

may trigger the decay of an excited electron. This decay

transition again may occur in one or in several steps and may

result in the emission of a photon. Stimulated emission may

occur <u>only</u> when the incident photon has the same energy as the photon that is released. This triggers a chain reaction with the result that one photon results in the release of two, and these two photons may stimulate the release of four photons. Thus, the final result is an increase in the photons of identical energy and in a simultaneous and in-parallel vector. Additionally, the photon that is released is temporally locked to the oscillations of the first photon. The final result is that the incident of photon and the emitted photon are coherent, monodramatic and spatially and temporally aligned. If all of the atoms in a lasing medium exist in an excited state, then the incident photon can initiate a cascade very similar to a nuclear fusion reaction. One photon can yield two, two photons can yield four and so on, on a chain reaction. This can only occur provided that all of the atoms in the lasing medium are at a higher energy state than the ground state. When more than half of the atoms in such a system are in the excited state, the system is said to be in population envision. Lasing can only continue when the atoms are kept in a population aversion. Should for instance, a lasing medium be brought up into an excited state, and then stimulated, this would result in one very brief, very intense pulse, and this is the mechanism of functioning for certain of the lasers which will be discussed later. If one wished to maintain a continuous wave output from a laser, then energy must be continuously applied to the system to keep the atoms in such a population inversion.

The direct emission of photons from such a stimulated system may be random. Photons may exit the system from the side walls, but some of the photons eventually are going to start traveling parallel to the long path of the lasing cavity. A laser is composed of lasing cavity with mirrors on either end to reflect these photons back into the system. These photons, traveling back and forth between the two mirrors, are able to continue this photon chain reaction occurring in a longitudinal axis and reinforce the laser beam by this method. Photons that are randomly scattered from the system and exiting from another direction other than long axis of the lasing medium, are then lost to the system and often converted to heat. This is the reason that many of these lasers need quite extensive cooling systems (either air cooled or water cooled systems). This is also the reason that most lasers have a very low operating efficiency. For example, for an efficient carbon dioxide laser has an operating efficiency of only 15% or less.

The two mirrors of this system may either be 100% reflective mirrors in which case the laser would continue to build up in energy within the tube until eventually the mirror was destroyed, or partially reflecting allowing a continuous beam. Another system uses a mirror in a shutter, and when the light to be released in one very strong pulse. This system which allows for a build-up of a very powerful pulse is employed in some of the Nd:YAG Q switch lasers and will be discussed later. Most often, one of the mirrors is totally reflecting while the other allows a

portion of the light to escape. This produces a continuous wave
beam (providing of coarse energy is continuously applied to the
system to keep the atoms in a population of inversion). There is
a precise relationship between the wavelength output and the
distance between the mirrors. The mirrors must be an integral
wavelength distance separate from one another. Otherwise,
standing waves within the system would serve to decrease the
output efficiency of the laser cavity.

The relationship between the energy and wavelength of a
photon is expressed via the constant in the following equation E
= HV where E is energy, V is the frequency and H is Plank's
constant (6.626 x 10 the ⁻34 Joule seconds). From this equation,
it can be seen that the energy in a photon is directly
proportional to the frequency. From the relationship LV=C where
L is the wavelength, V is the frequency and C is the speed of
light, it can be seen that the frequency is inversely
proportional to wavelength. The implications here are that short
wavelength ultraviolet and blue light have higher energy than
longer wavelength red or infrared light.

The relationship between energy and wavelength is very
important. When considering both the absorption and emission of
light by an atom or molecular species, if the transition from the
ground state to the excited state requires an amount of energy
that is equal to the energy in an incident photon, then that
photon is easily absorbed. Conversely, the energy decay back to
a ground state is accompanied by the emission of a photon of

specific wavelength based on the energy and the transition. The implications from this are that different species of atoms have different absorption spectra and thus the emission spectra, (or laser output wavelength). Specific atomic and molecular species are unique and possess discrete energy characteristics for each electron orbital.

Characteristics of Laser Light

From the previous discussion, it can be seen that the mechanics of generating a laser beam results in the generation of light that is unique from normal light. Normal light such as that from the sun or from a light bulb is composed of multiple wavelengths traveling in various directions at different time frames. Laser light has three basic characteristics that are unique. One, laser light is monochromatic. Since the photons are emitted from a homogeneous population of atoms or molecules, all must come from the same energy transitions. These photons are all of identical wavelength. This monochromaticity is unique to lasers and enables tunable lasers to target specific biomolecules having absorption at that characteristic wavelength. Two, laser light is coherent. All of the photons in a laser beam, because they are stimulated by the same initial photon, oscillate together _in phase_. This coherence of the output of photons permits focusing the beam into a very small spot to create extremely high power densities. Three, laser light is collimated. Because of the design of the laser cavity, the output energy is concentrated into a narrow minimally divergent

beam. For example, in a surgical CO_2 laser, the beam can be directed down the center of a long articulated arm to be focussed at the end by lens and hand piece or a micromanipulator. Because there is minimal diversions of the beam, there is very little energy lost in this transmission within the articulated arm.

Timing of the Laser Beam

The laser beam can either be continuous (i.e. on all the time) or may be intermittent or pulsed. Laser pulses can be generated from the femtosecond (10^{-15} second) all the way up to multiple seconds of pulses by several different means. These mechanisms of pulsing a laser beam range from physical pulsing by means of a shutter, to pulsing the energy input into a laser medium, to using a optical shutter within the cavity to release all of the energy at a short-time duration.

Nanosecond pulses are generated within an Nd:YAG laser through a mechanism called Q-switching. This is most commonly used in the ophthalmologic lasers. The flash lamp within an Nd:YAG laser stimulates the YAG crystal to generate the laser pulse. At either end of the YAG crystal is a 100% reflective mirror. In the simplest of Q-switching cases, one of these mirrors is rotating very fast and constrains the laser output within the cavity. As the mirror rotates, a open window eventually crosses across the cavity and releases the laser energy. This releases all of the stored energy in one burst of power. Another method of generating Q-switching is to put an optical shutter within the cavity that reflects light until a

higher enough energy level is obtained. At this point, the chemical shutter undergoes a phased transition which allows the energy to escape. The result of each of these methods is that very high powers are generated with very short pulse durations. Such high levels of energy directed into very small volumes can disrupt the structure of materials and cause damage via electromechanical or acoustic shock. The practical application of this is for capsulotomy after cataract surgery.

Some pulsed lasers get their timing parameters from the timing of the pump source. The original flash light pump Ruby laser invented in the 1960's produced its laser output beam in this manner. For every flash of the flash lamp the chromium atoms within the Ruby laser are pumped into an excited state and spontaneous decay triggered the stimulated emission resulting in a brief flash of laser light. Repetitive pulses can be generated at the rate determined by the cycle time of the flash lamp.

Most gas laser which can function in the continuous mode use a mechanical shutter to modulate the beam. This is a impervious metal plate that fits across the beam path and is opened only when the actuating foot switch in engaged. This system is the most common system in use in the Argon and CO_2 lasers and is fail safe feature also found in most medical laser systems as a safety switch. Shutters are usually accurate down to 50 milliseconds, although some are capable of functioning much faster than this in experimental lasers. A unique phenomenon with the CO_2 laser is the super pulse mode. Pulses on the order

of microseconds are generated by pumping the laser cavity either with radio frequency energy or high peak power electric current. The energy is not stored within the cavity but is released at the time of generation and the repetition rate is determined by the cycle time of the energy input source. Powers on Medical CO_2 lasers as high as 1 kilowatt may be generated at intervals. The repetition rate of the pulse generation may vary from two pulses per second to as high as 5,000 pulses per second on some lasers. The total energy delivered to the tissue is a function of the pulse duration and the repetition rate. In general, the more pulses delivered to the tissue, the higher the average power applied to the tissue. Further discussion of super pulse is covered in the section on (laser tissue interaction).

Types of Lasers

Given enough energy input, almost any material can be made to undergo stimulated emission. Newer medical lasers are now being designed from the application standpoint initially, as opposed to early laser design. Early laser design was on the order of "generate the laser beam and lets see what it does with tissue." Now, however, surgeons are able to request a wavelength and the physicists are able to build a laser with that specific output. Unfortunately, sometimes the efficiency of energy conversion is not very good and the output energies are sometimes too low to be medically useful, but do provide some interesting data within a laboratory setting. Lasers are generally identified by the nature of the laser medium. This laser medium

can exist in a solid state as in the Nd:YAG laser, within a liquid state as within the Argon pumped dye laser, within a gaseous state as in the CO_2 laser or as an ion in the Argon laser. In addition, two lasers which are just beginning to have medical application, are the Excimer laser in which a chemical reaction generates the laser beam and the Free Electron Laser in which the lasing medium is actually excited electrons. A partial listing of some of the lasers that have been tested for medical applications is included in Table X. For brevity, we will discuss only those lasers in most common use in Otolaryngology-Head and Neck Surgery at the present time, and make note of some of the potentials of the newer lasers.

Carbon Dioxide Gas Laser

The carbon dioxide laser actually uses a mixture of nitrogen, carbon dioxide and helium gasses in its cavity. Energy can be applied to the carbon dioxide laser either by radio frequency or direct current. Direct current can be applied either longitudinally down the cavity or transversely across the cavity. While transversely excited carbon dioxide lasers are capable of generating very high peak powers on the order of kilowatts, these lasers are generally reserved for commercial applications as they require careful alignment and maintenance. Most CO_2 lasers today now use radio frequency and sealed tube systems, some of the earlier lasers were flowing gas systems which required constant replenishment of the laser mixture, because with continued applied energy some of the carbon dioxide

atoms are eventually broken down into component atoms. Energy
applied to a carbon dioxide laser cavity is initially absorbed by
the nitrogen molecule. The decay of energy from the nitrogen
molecule then allows transfer of energy to the carbon dioxide
molecule. Specifically, the output energy of 10.6 microns
represents one of the bending frequencies of the CO_2 molecule.
Helium gas helps to dissipate the heat from the laser cavity.
Because the carbon dioxide lasing medium is a molecule, there is
the capability for these lasers to produce a wide range of
possible energy level transitions and therefore wavelength
output. The wavelength of 10.6 is the most efficient output for
the CO_2 laser and efficiencies on the order of 20% are possible.
It is fortuitous that the CO_2 laser invented in 1964 is absorbed
well by water and since tissue is composed of between 70 and 85%
water, this laser has now become the workhorse laser in
medicine. The specific reactions of the CO_2 laser with tissue
are covered more fully under the section (Laser Tissue
Interaction).

Argon Ion Laser

This laser uses charged argon ions as the lasing medium.
Because argon ions have such a diffuse range of energy levels
available, this laser gives rise to a composite laser output with
several visible wavelength created simultaneously. The
strongest emissions are at 488 nanometers and 514 nanometers,
although there are several other output wavelengths that are
easily identified on spectroscopy. Each wavelength may be

selectively filtered out to give a monochromatic beam if desired and the green wavelength is commonly used by ophthalmologists for retinal photocoagulation. Argon lasers are generally much less efficient than CO_2 lasers because much of the energy input into the system must be used to generate the argon ion, and then further energy must be applied to stimulate the ion to a state of population inversion. Inherent in all of this energy input is high heat generated, and most argon lasers need to be cooled by flowing water. Medical argon lasers are now capable of producing on the order of 20 watts and their beams are capable of being transmitted to via quartz fibers.

Dye Laser

There are two dye lasers in common use within medicine currently. One is the Argon Pumped Dye Laser, and the other is the Flash Lamp Excited Dye Laser (FEDL). In the Argon pumped dye laser, an argon laser is used as the input energy source to initiate the stimulation of the dye molecules. In the Flash Lamp Excited Dye Laser, a flash lamp performs the same function. Within the laser, the dye is constrained within a cavity and energy placed into the dye results in a population inversion and generation of the laser beam. Because the dye is a complex macromolecule, the potential exists for multiple wavelength output. In practice, once the dye is energized it often lases at multiple output frequencies simultaneously. The output from a dye laser is then directed across a diffraction grating which allows the selection and tuning of one particular wavelength

(usually accurate within 1/2 to 2 nanometers). Because of the design of the cavity, dyes can be changed to allow a wide range of tunability for output wavelengths and the selection of dyes that are efficient in the particular wavelength under consideration.

Nd:YAG Solid State Laser

The Nd:YAG laser is a solid state laser using the rare earth element neodymium in a crystal composed of yttrium and aluminum in a garnet arrangement. This laser is stimulated using a flash lamp and, although the output appears continuous, in reality it is a quasi-continuous laser. Quasi-continuous lasers function with repetition rates so fast as to appear to be continuous for all intents and purposes. The output of the Nd:YAG laser is in the near infrared at 1.064 microns, but because of the arrangement of the crystal other outputs are possible from this same laser. It should also be noted that the neodymium glass laser was invented first and has an output of 1.060 microns. This output demonstrates an important point in the physics of lasers in that the environment surrounding the lasing material may alter the output wavelength by placing constraints on the energy level transitions available. Most YAG lasers initially were water cooled because of the high heat generated, but most recently several medical YAG lasers have come on the market which are air cooled with power capabilities in the 100 watt range.

Frequency Doubled YAG

Several years ago when argon lasers were not capable of

producing power outputs in the deep coagulation and vaporization range (i.e. above 8 watts) a technological variation of the Nd:YAG laser was produced. This unit was known as the KTP 532 system. In this unit, a YAG output wavelength of 1.064 microns was directed through a potassium (k) titanium (T), Phosphorus (P) non linear crystal. This crystal has the unique property of doubling the frequency of the laser beam (thereby cutting the wavelength in half). This laser was capable of generating out approximately 17 watts of power from a 100 watt YAG input power. Its output is therefore in the green wavelength and falls intermediate between two of the major absorption bands for hemoglobin. There are other crystals which exist which can triple the Nd:YAG frequency and produce wavelengths in the near ultraviolet region at 354 nanometers, but these have not seen extensive medical use yet.

Excimer

The term excimer is a contraction of the words "excited dimer". Molecular dimers such as argon fluoride or zenon chloride are used to produce the laser beam. Outputs are ultra short pulses in the near ultraviolet range at wavelengths from 157 to 351 nanometers (please see table). Due to the extreme short pulse duration and the high energy of ultraviolet wavelengths, the effect of the excimer laser is photoablative. Photoablative effects can work by physically disrupting the molecular bonds within tissue. This will be covered further in the section on laser tissue interaction.

Equipment Requirements

Each laser will have unique power, water and maintenance requirements which should be carefully considered before purchase and installation in the operating room. Many times, medical lasers require modifications to the operating room that need to be in place before a laser can be used, and this may unnecessarily delay the start up of the medical laser. Certain lasers require specific water and electrical modifications to specific operating rooms. In addition, certain lasers are too large to be easily transported between rooms, therefore one operating room should be dedicated as a laser operating room. Some carbon dioxide lasers are low power (generally less than 40 watts and usually less than 40 to 60 pounds using 110 volt 28 amp power). These lasers are self contained and most often air cooled. The higher power CO_2 lasers have self contained water cooling systems and do not require external cooling, although some of the higher power CO_2 lasers use two 110 volt, 20 to 30 amp circuits: one for the cooling system and one for the laser. Most carbon dioxide lasers on the market at the present time are sealed systems which means that no external tanks need to be attached to the CO_2 system to generate the laser beam, although some of these lasers do require an external nitrogen purge gas system to be attached. Sealed tube systems have a fairly long life-time in the current lasers and, because of the stability and ease of use, most manufactures have switched to this type of system.

Nd:YAG lasers due to their inefficiency usually require 220 volt AC 40 to 60 amp power, although some newer units on the market are now powered with 115 volt circuitry. Older Nd:YAG units often needed an external water source for cooling, but the newer units that are available up to 100 watts of power are now available with internal cooling systems. These older high powered YAG lasers, the KTP laser and the Argon laser all require a source of cool water to operate the system. Flow rates of several liters per minute are often required. In addition, a separate consideration in the south is that tap water may not be cool enough and built-in interlocks within the lasers will shut the system down. Often, an inter-cooler needs to be installed so that the tap water can be run through an air conditioning unit to make it cool enough to allow the lasers to be used. All these requirements should be considered before purchasing a laser and before having a laser shipped, so that the operating room and related facilities are ready for laser use.

Laser Delivery Systems

The beam emitted from a laser tube is a collimated monochromatic coherent beam of light traveling in a straight direction. Some mechanical system must be employed to re-direct the beam in a useful fashion so that it can be used for medical applications (the alternative is to move the patient underneath the beam itself).

Hand Held Laser

Helium neon laser pointers, gallium arsenide diode lasers

and one brand of a low output (less than 20 watt CO_2 laser) can be held in the hand like a pencil. The beam is directed to the tissue without any delivery device except for a focussing lens. Diode array lasers are now capable of providing power up into the watt range and experimental systems using diode lasers through non-linear crystals can provide a variety of wavelengths with powers around 1 watt.

Articulated Arms

Mid and far infrared lasers such as the carbon monoxide and carbon dioxide lasers use an articulated arm system to deliver the beam. This is because there are no FDA approved optical fibers at the present time capable of transmitting in this wavelength. The laser beam is directed down the center of a series of hollow tubes with mirrors positioned at the ends to reflect the beam at 90° angles. Mirrors are mounted in a gimble joint to allow free rotation in three dimensions. The articulated arm then can be attached to a hand piece, microscope or bronchoscope adapter, or the newer CO_2 wave guides (please see below). Some of the hand pieces provide a variable spot size and obviate the need for moving the hand piece away from the tissue to de-focus the beam. The accessories attached to the end of an articulate arm often need the accessory nitrogen gas purge system to keep the laser plume from fouling the reflective mirror or lenses. The articulated arm is able to maintain both monochromaticity and coherence of the laser beam unlike fibers or wave guides.

Optical Fibers

Most lasers from the near ultraviolet up through the near infrared (including the visible spectrum) are capable of being transmitted through small diameter flexible fibers. The advantage to these fibers is that they may be inserted through endoscopes to deliver energy deep into the body. This has been one of the major advances in the use of lasers, and smaller and smaller fibers are now permitting the use of lasers to re-canalize blocked coronary arteries and peripheral veins. Some of these fibers while being only 2mm in diameter, also employ a visualization system as well as the laser delivery system.

Quartz silica fibers transmit light energy from ultraviolet to near infrared wave lengths, and thus this material is useful for delivering energy of Excimer, Argon, KTP, dye and YAG lasers, but unfortunately are not capable of delivering the output from a carbon dioxide laser. Fibers that are capable of transmitting the carbon dioxide wavelength are in the developmental stage and several are on clinical trials right now. Materials include tellurium bromide and silver iodide, but these materials are very fragile and tellurium specifically is toxic to the body and thus a bio-compatible cladding which protects the body from this material has to be developed. These fibers have a very complex crystal matrix and have a limited bend radius before cracking, but still are capable of maintaining a tighter bend radius than the hollow wave guides that have currently been developed for the CO_2 laser (please see below).

These quartz fibers alter the characteristics of the laser beam. The beam is reflected multiple times within the fiber due to the difference between the optical coefficiency between the fiber itself and the cladding. Because of the multiple reflections within the fiber, although the beam remains monochromatic, it looses its coherence. Most fibers do not employ a focussing lens at their terminal end, and therefore the beam diverges fairly quickly once it leaves the fiber. This divergence is a function of the optical material and the size of the fiber and can range from 8° of divergence to as high as a 30° divergence. The implications for this range of divergence are that the fiber must be held closer to the tissue to maintain high enough power density to be able to perform vaporization and or coagulation. For most endoscopic applications, the end of the fiber is cleaved smooth to provide and even distribution of light output, so that there is no hot spot generated. Another point should be made about using the fibers with endoscopes is that because of the divergence of the beam as soon as it leaves the fiber, if the fiber is accidentally withdrawn within the endoscope, the rapid divergence of the laser beam can be responsible for melting the tip of the bronchoscope (a very expensive mistake). Thus, when using a laser endoscopically, it is imperative that one can see the fiber and the point to be vaporized or coagulated at the same time to avoid this mistake.

Contact Tips

The development of a tapered lens made of silicone or

synthetic sapphire allows the re-focusing of the laser beam from the end of the optical fiber. This advantage of returning a lens system to the optical fiber actually can allow one to concentrate the laser beam into a smaller diameter than that carried through the optical fiber itself. These optical fibers are available in various shapes and lengths and use silica lenses for Argon applications and generally synthetic sapphire for Nd:YAG applications. These contact tips come in several shapes and sizes and the shape determines the concentration of the light energy. A very long tapering point brings the laser energy into a very concentrated point for cutting and with this lens in contact with the tissue, this serves to cut through tissue "like butter". If the tip is not held in contact with the tissue however, the laser energy has limited methods for dispersement and can actually vaporize the tip of the lens, effectively ruining it. These contact tips can be very expensive running from $150 to $600 dollars apiece for specialized shapes. Other shapes that are available include a chisel tip that are allows one to shave layers off a tissue from a obstructing tumor, and frosted tips which are capable of dispersing light at all angles which are especially effective at coagulation.

Wave Guides

Several manufactures have recently introduced hollow wave guides which can be used to transmit the 10.6 nanometer light from the carbon dioxide laser. These wave guides range from 3mm in diameter down to 2.7mm in diameter and have some limited

flexibility, although the size and capability for bend radius limits their applications to generally free hand work. They are not capable of being placed down a flexible endoscope. Gynecologist were among the first to explore the capabilities of these CO_2 wave guides inter-abdominally and newer advances in these wave guides have seen their adoption by orthopedic surgeons for arthroscopy and potentially by otolaryngologist for intranasal work.

Microscope and Bronchoscope Adapters

The near ultraviolet, visible and near infrared wavelengths can be transmitted through fibers and therefore can be passed down the side channel on ventilating bronchoscopes or down the operating channel in flexible bronchoscopes. For laryngoscopy work and for otologic work hand, held probes composed of these fibers may be used. The KTP laser also has a microscope adapter which functions by bringing the laser beam into the adapter via a fiber and then this is reflected off a mirror and redirected into the operating field. A necessary modification for each of these units is an eye piece filter to protect the surgeons eyes while these lasers are being used.

The carbon dioxide laser beam because it cannot be passed through a flexible fiber is often directed down the center of a rigid ventilating bronchoscope either as a collimated beam or through a rigid wave guide. When the laser beam is directed as a collimated beam, the articulated arm is connected to a bronchoscope adapter, but employs a beam splitter to redirect,

laser beam and allow visualization of the target simultaneously. The aiming beam is also re-directed to allow the surgeon to plan the laser impacts. The nitrogen gas purge system is used to remove laser plume and smoke from the operating channel of the bronchoscope. The microscope adapters (also called micromanipulator) allow lasers to be used for laryngeal, otologic or precise microscopic control of laser beam. The micromanipulator has a gimble controlled mirror assembly that is attached in front of the objective lens of a microscope. As mentioned before, the KTP laser delivers the beam to the micromanipulator by means of a flexible fiber and the CO_2 laser directs the beam to the micromanipulator by means of the articulating arm. Either the mirror itself or another lens with a micromanipulator is used to focus the laser beam. Microscopic focal lengths from 200 to 400mm may be selected allowing use from the standard otologic operating distance all the way out to the standard laryngeal operating distance. Because of the variation in focal length, the spot size of the laser also varies. In the traditional micromanipulator (prior to those developed about 1989) the smallest spot size capable at 400mm focal length was approximately 750 microns while the spot size at 200 microns was approximately 350 microns in diameter. This spot size is a function of both the focal length and the wavelength of the laser beam itself. In general, the shorter the wavelength of the laser the tighter focus can be obtained. The newer micromanipulator recently developed for use with the carbon dioxide laser are now

known as "microspots". These microspots are capable of yielding
a focused beam of 250 micron diameter at 400mm and 125 microns at
200mm when properly focused. This has implications for the
amount of power that is necessary to be used and will be covered
later under the section on laser tissue interactions. A
potential difficulty with some of the older micromanipulator for
use with the carbon dioxide laser is a concept known as
parallax. The carbon dioxide laser beam as it emerges from the
lasing tube is broad, and a larger mirror than that used for a
fiber is used to redirect the beam. The size of this mirror is
limited to the inter-pupillary distance on the microscope and
oftentimes this is not big enough to redirect the entire CO_2
beam. If the mirror was large enough and placed inter pupillary,
it would then interfere with the nasal field of view for both
eyes. Many of the micromanipulator in use bypass the mirror size
limit by off setting the mirror below the plane of vision by
almost to 1 to 1 1/2cm. This allows them to use a large enough
mirror to redirect the beam. The difficulty with this
engineering design however, is that when used in tight areas such
as laryngoscopy in children when using a subglottiscope with
limited vertical height, this discrepancy between the plane of
view and the path of laser beam may lead to inadvertent burns to
the patient near the lip of the laryngoscope (Figure X). The
newer microspots and the some of the newer micromanipulator from
some of the companies employ a different optical system using a
"hot mirror" assembly. This hot mirror is specially coated lens

which is able to reflect the far infrared wave length of the CO_2 laser while also allowing visible wavelength radiation to pass through. Therefore, the object to be hit with the laser beam can be visualized through this lens assembly while the CO_2 beam is reflected off of this assembly allowing coincidence of optical path and laser path. This allows the laser the be used in much tighter areas such as through an otologic speculum or a neonatal subglottiscope.

Aiming Beam

The Argon, KTP, helium neon, gold vapor and visible dye wavelengths all by nature work in the visible wavelength range of the spectrum and an attenuated version of their output beam can serve as their own aiming beam. Lasers in the ultraviolet and infrared regions such as the Excimer and the Nd:YAG and CO_2 laser emit invisible radiation and therefore need an aiming beam to allow the surgeon to select the impact site. The Nd:YAG often uses an attenuated output from the Krypton or zenon arc lamp which appears as a very bright spot when aiming this unit. Alternatively, some manufactures have added a helium neon laser to be used as a guide beam for the Nd:YAG laser. In the CO_2 laser oftentimes a helium neon red laser is used for the aiming spot. This is often a 5 to 10 milliwatt small Class IV laser unit. When using either system, it is important that prior to patient application, test spots should be fired to assure that the burn created by the operative beam coincide with that from the aiming beam and are of known size. Because the helium neon

beam is generally of shorter wavelength than the YAG or the CO_2 beam, the aiming beam is much smaller than the resultant impact.

Potential difficulty arises here with the use of the red helium neon laser as an aiming spot in a bloody field. The helium neon beam is often very difficult to pick up against a red background. Manufactures have tried to overcome this by including more powerful helium neon lasers as part of the aiming package, but potential difficulty is reached when the power for the helium neon is bright enough that the glare is potentially painful to the surgeons eyes. One system to overcome this aiming problem would utilize an aiming spot in the green or yellow wavelengths, and although these systems are currently being testing and on the production drawing board, there are no medical systems available yet which use a green or yellow laser aiming spot.

Basic Laser Tissue Effects

Beam Profile

The measurement of the energy output in a cross section across the beam from most medical laser systems would reveal a gaussian or bell shaped distribution of power. This beam profile has the highest power concentration at the center and drops off exponentially as one moves further away from the center of the beam. For practical purposes, the radius of the spot for a gaussian distribution beam is to find the distance from the center to the point where the power has decreased to $1/e^2$ peak power. In fact, this defines the portion of the gaussian curve

that contains 87% of the total power and is defined as the spot size. This holds true for most medical lasers when viewing the beam as it is emitted from the laser cavity. However, once a beam has been transmitted through a fiber, or reflected off mirrors, the spot can change to a non-gaussian distribution beam profile. In addition, certain lasers produce beams in non-gaussian profiles directly from the cavity. These spots have a much steeper rise to a peak with a flattened top similar to a "top hat". When defining the tissue effects it is most appropriate and meaningful to define the spot size in terms of square centimeters or radius. This would allow one to directly calculate power densities and energy density.

Beam profiles are also specified by their transverse electromagnetic mode (TEM). A TEM_{00} is considered the fundamental mode and is a gaussian distribution. Higher modes (TEM_{01} and TEM_{10}) produce a power distribution that can be described as a doughnut with a relatively low powered section in the center. A TEM_{11} has an essentially rectangular distribution and can be represented as a "top hat" profile. The smallest spot sizes are achieved with a gaussian distribution (TEM_{00}). As (TEM) mode increases, spot size also increases, therefore decreasing power density (see below).

Power Density

Due to the nature of laser light being coherent and collimated, the laser beam can be focussed into extremely small spot sizes with the possibility of creating very large power

densities. The laser can be focussed into a spot of less than one micron in diameter (depending upon the wavelength and focal length of the lens) and thus is capable of generating the power densities that are equivalent to the energy available at the surface of the sun. Power density is defined as the power (or watts) over area in square centimeters (see Figure 3). For a constant power output, from the equation it can be seen that the smaller beam spot size i.e. the smaller the area, the greater the concentration of power. This follows the inverse square law. The area increases as the square of the diameter increases. The following table illustrates the relationships among spot area and power. Notice that a lens system that is capable of delivering a 50 micron spot can produce power densities of one million watts per centimeter squared with only a 20 watt power input. Another relationship which can be visualized from the table is that achieved by focussing or de-focussing the hand piece. If the spot diameter is increased, then the power density decreases by a exponential factor. For example, if the spot diameter is doubled, then the power density will decrease by a factor of 2^2 or 4. If the spot diameter decreases by half, then the power density would increase by 4. When the beam is de-focussed, the spot diameter increases and this decreases the power density geometrically. Because of this relationship between power and spot to produce a power density, it is important to communicate the spot size and the input power when describing tissue effects.

All laser delivery systems have an optimum focal distance responsible for the smallest spot size. In general, this is the usual working distance for the hand piece or for the micromanipulator. However, there exist situations in which it is necessary to have a broader beam, as for coagulation or with higher powers for vaporization of a larger surface area. This is accomplished by defocusing the beam or prefocusing the beam. When using a hand piece, defocusing is done by simply pulling the hand piece further away from the tissue, therefore removing the focal spot away from the tissue and broadening the beam. On micromunipulators and on bronchoscopes, there is a defocusing lens which is used to accomplish the same purpose. Defocusing, as can be seen from the table above, results in a lower power density and therefore is more effective for coagulation given the same input power. The focal spot from a hand piece can also be enlarged by bringing it closer to the tissue, called prefocusing. This results in the focal point being projected beneath the surface of the tissue and may cause uncontrolled damage deep in the tissue. The effect is that the overlying tissue is vaporized fairly slower because of the lower power density and as this tissue is ablated and it comes closer to the focal spot itself, the power density increases and the rate of vaporization also increases, making control of this technique very difficult.

Understanding the concept of power density is sufficient for working with the CO_2 laser and other lasers which have immediate tissue effects, but tissue effects generated by some lasers are

not always immediately apparent. For example, the extent of deep
thermal necrosis from the Neodymium:YAG laser is a function of
laser power and the time the laser is in contact with the tissue.
Some of these effects only become visible 24 to 48 hours after
laser impact. This is not to say that laser tissue interactions
are totally unpredictable. As a matter of fact, the amount of
necrosis can be predicted but only if the total light dose
delivered to the tissue is known. The inter-relationship of
laser power spot size and duration of effect on duration of
exposure to tissue is represented in the following figure. The
output power from the laser is measured in watts. The amount of
energy applied over time is energy (Joules = watts x seconds).
Energy density (Joules per square centimeters) is a composite
measurement of the power duration of exposure to tissue and spot
size. Within medicine, energy density is referred to as light
dose by the clinician, and physicists refer to it as fluence.

Tissue Optics

An overview of the effects of light interacting with tissue
is represented in Figure 4. For this initial discussion of basic
tissue optics the effect of wavelength and the rate of energy
delivery to the tissue will be postponed until later.
Progressing from the surface of the tissue inward, we will
discuss reflection scattering transmission and absorption, and
the various interactions that can occur between and among these
properties. Light incident upon tissue can be reflected from
the surface of the tissue. The minimum amount of reflectance

occurs when the incident light is directed orthogonal to the tissue. As the angle of the light incident to the tissue decreases, more and more light may be reflected from the surface. In clinical application, this is important because most surgeons have a tendency to hold a laser hand piece at an angle to a tissue like a pencil. There can be significant reflection and therefore decreased power delivery to the tissue but also, the spot will form an oval instead of the smallest focal spot (circle). Awareness of the concept of reflection is also important when a laser is used in a lumen such as in the trachea or bronchi. The beam in this instance may achieve a very low angle of incidence with the wall and the energy may be reflected to a remote site and damage may occur to normal tissue. This effect is clinically more commonly seen with the Nd:YAG than with the CO_2 laser.

Light may also be reflected from internal components of the tissue, including atoms, molecules, and macromolecular structures. Multiple reflections within tissue is termed scattering. At any point, light may be reflected back out of the tissue and this results in what is called diffuse reflectance. Clinical application of this principle is in reflective pulse oximetry. Here, a diode directs light into tissue and the reflective light is measured for spectral absorption or changes, giving a relative measure of the oxygenated hemoglobin to the de-oxygenated hemoglobin ratio, since these two forms of hemoglobin have different absorption characteristics.

Light may also pass completely through tissue without any interaction with any of the tissue material. This is very uncommon and in fact the only wavelengths that can commonly pass through the body are cosmic rays. Visible light and all medical laser wavelengths are eventually reflected or absorbed within tissue, although some wavelengths are able to penetrate deeper before this effect occurs. The concept of light passing through tissue without an interaction is called direct transmission and for most medical lasers is limited to a millimeter or so within tissue, but may extend to as deep as 3 or 4mm for the Nd:YAG laser. The most common form of transmission of light through tissue is called diffuse transmission. This results from light that is scattered or multi-reflected within tissue that may be eventually transmitted deep within the tissue. The total of the through transmission and diffuse transmission is simply the transmission of light through tissue. A clinical example of this effect is trans illumination of a sinus with a very bright light. The diffuse red glow is the transmittance. Another example is the transmission of light through a finger. If the light is bright enough, the bone can actually be seen and this concept is now being developed for detection of breast masses and is known as diaphanography. In this technique, the breast tissue is supported as in a mammogram and then the intense light is transmitted through the tissue. There is no radiation in the basic procedure, but unfortunately at the present time, the sensitivity and specificity is not high enough. Another clinical

destruction when illuminated at one wavelength, but when illuminated at another wavelength, undergoes a fluorescence. This property of fluorescence is being investigated for the possible detection of metastases within tissue. Another potential application is the illumination of tissue, blood or serum looking for the fluorescence of specific target macromolecules. The concept here is that if one were able to identify a specific protein antigen such as carcinoembryonic antigen and were able to identify a specific fluorescence spectrum present in serum, this would afford a very quick screening test for this tumor marker.

Wavelength Dependence of Tissue Interaction

In general, light must be absorbed by a molecule or tissue component to have an effect. As demonstrated in the section on tissue optics, this absorption can cause effects of heat, or florescence, or optical breakdown of that particular compound. These compounds are also known as chromophores. The major tissue chromophores are water, melanin and hemoglobin. Each of these chromophores exhibits a complex absorption spectra as represented in Figure X. Melanin shows a gradually decreasing absorption as one increases in wavelength. Water demonstrates a relative window or lack of absorption in the visible wave ranges and hemoglobin is more strongly absorbed in the blue-green region. It can also be seen that the strongest absorbing chromophore is water, and the most efficient peak for absorption occurs around 3 nanometers. The absorption of the CO_2 laser energy at 10.6

microns is accounted for in the molecular transition and
vibration modes of water. Since water is one of the most
efficient absorber of energies, and given the fact that the
tissue is largely water, this means that laser energy is absorbed
very efficiently and penetrates very little in the 10.6
nanometer wavelength. The energy from a CO_2 beam is absorbed in
a very shallow distance at the surface of the tissue, vaporizing
the surface water and then proceeding to be absorbed by the next
layer down and so on. The interaction of laser through the
thermal interaction with tissue then can be thought of as a
sequential process where the laser vaporizes the superficial
tissue proceeding deeper into the structure. Because of the high
heat diffusion capability of tissue due to the water content, the
thermal spread ground the CO_2 laser impact area is limited
somewhat. The thermal affect has been estimated to range from 50
to 250 microns surrounding the point of impact of the CO_2 beam.
Better absorption of water occurs at round 3 nanometers, and
several lasers are being tested to take advantage of this very
high absorption. The Erbium YAG laser at 2.94 microns is one of
these, and because of the higher absorption of energy, and
therefore the relative lack of penetration, the thermal damage
surrounding the zone of vaporization is even less for the Erbium:
YAG laser (as small as 2 microns for the thermal effect
_____ for the Erbium YAG compared to 11 microns for the
CO_2. Bone is composed of less water and, therefore, reacts less
to a CO_2 beam. However, the Erbium YAG laser in particular has

been shown to be somewhat effective for cutting through bone. The CO_2 laser creates a ring of black char where the temperatures can reach several hundreds of degrees surrounding the zone of laser vaporization. This is not seen with the Erbium:YAG lasers.

There are several medical laser in the visible wavelengths, including the argon, KTP and Flash Lamp-Pump Dye lasers which all take advantage of absorption by hemoglobin and melanin. These lasers effective pass through the superficial lasers that are transparent to these wavelengths because of their high water content and are preferentially absorbed by hemoglobin and melanin in the connective tissue layers. Because of the absorption of energy by blood, these lasers can be used to effect coagulation within the vasculature. Hemostasis with these lasers is excellent. The Pulsed Yellow Dye Laser is more highly selective in targeting hemoglobin to the exclusion of other skin chromophores (melanin) and has found widespread application in photocoagulating port wine stains. The KTP and argon lasers due to some of their absorption with melanin are less specific for these applications.

An "optical window" exists in tissue from approximately 600 to 1800 nanometers, due to the relative drop-off in absorption for melanin, hemoglobin and lack of absorption for water. In this region there is no major tissue chromophore and light will pass deep into the tissue and scatter widely. The Nd:YAG laser wavelength of 1.064 nanometers occurs within this window and as a

result, this laser penetrates very deeply and scatters widely.
The clinical effect is that this laser can raise the temperature
of a large volume of tissue effecting coagulation and tissue
thermal effects as deep as 4 to 5 millimeters under proper
conditions. Thus the Nd:YAG laser is good as a coagulator, but
is not as efficient at vaporizing tissue unless the power
densities are increased into a very high level such as can be
accomplished by focusing the Nd:YAG to the tip of a contact
fiber. The red wavelengths of light used for photodynamic
therapy (630 nanometers) and for laser biostimulation with the
Helium Neon laser (632.8 nanometers) are also within this region
of relatively deeper tissue penetration.

Tissue Response to Light

The response of tissue to light is dependent upon several
factors. The first factor is wavelength, but in addition, the
power or total energy applied, and the rate of time over which is
energy is applied, and the duration of light application are also
vitally important in characterizing the response of light with
tissue. Total light doses of between 1 and 10,000 Joules per
centimeter squared are most commonly used for biological effect.
It should be apparent that the same light dose may be delivered
by very high intensity brief flashes or by low intensity
illumination over a very long period of time. Each of these
results in very different tissue responses. Very low levels of
light energies applied over long periods of time have the

potential to drive photochemical reactions such as
photosynthesis. On the other hand, focusing laser energy into
very small spots creating very high power densities and applying
this energy over a very short time can result in extreme thermal
effects within the tissue. Sometimes these thermal effects are
so high as to generate plasmas within a tissue. The interaction
of light with tissue can be broken down into four basic types of
reactions. Photochemical, thermal, photoablative and
electromechanical reactions.

Photochemistry

Low levels of light energy applied to tissue over long
durations of time can result in photochemical reactions.
Photosynthesis is a common example of this. In photosynthesis,
photons are absorbed by chlorophyll molecules and plant
chloroplasts and eventually converted into a photon concentration
gradient driving the synthesis of adenosinetriphosphate.

The experimental treatment for cancer, photodynamic therapy
(PDT) is an example of clinically useful interaction of light
with tissue on a low energy level. In PDT, a light absorbing
chromophore such as the drug Hematoporphyrin Derivative, (HpD),
is the compound responsible for light absorption. HpD is
preferentially localized in malignant and embryonic tissue
following systemic injection. Once the drug has localized
within the tumor, the tissue is illuminated with light on to one
of the absorption peaks of hematoporphyrin derivative.

Fortunately, HpD has a moderately good absorption peak at 630 nanometers (red light) which allows moderately deep penetration of light into the tissue. Please see Figure X. The reaction in photodynamic therapy depends upon the presence of the molecule of HpD, light of the proper wavelength, and molecular oxygen. The interaction of these three initiates a photochemical reaction. The photon of light stimulates HpD to a high energy level and through a series of electron tranferances singlet oxygen is produced. Localized tumor necrosis is a result of oxidation of the host tissue by this singlet oxygen. In this reaction, the light that is applied to the tumor is given in such a low rate of fluence that there is no thermal effect resulting from the use of the laser. Areas of normal tissue that do not contain metaporpharine derivative are spared. However, most tissue does retain some HpD to a slight extent for up to six weeks after application, and the major side effect of is photosensitivity to sunlight.

The concept of laser biostimulation was originally advanced in Europe and in Asia and is being currently investigated with applications in wound healing, chronic pain and arthritis. The mechanism of action of low level light interaction with tissue to bring these changes about has not been well worked out yet, but may be related to a similar mechanism as is found in acupuncture. The effects on wound healing (i.e. faster wound healing) and on arthritis (decreased inflammation and increased joint motion) potentially may be mediated by a reaction with mitochondria. It

has been suggested that absorption of light by respiratory enzymes in mitochondria can be converted into chemical energy such as ATP. The rationale for this being that mitochondria probably started as a purple algae, and retain the ability to undergo a basic form of photosynthesis. As stated before, the mechanism has not yet been completely worked out.

Non-thermal Laser Tissue Effects

Photoplasmolysis

At the upper end of the power density time continuum is photoplasmolysis. In this application, very high energies of light are applied to a tissue and focused into very small areas over a very short duration. The extremely high energy levels results in a plasma formation within tissue with the electrons being stripped away from component atoms generating the plasma. This field of plasma then expands throughout the tissue generating an acoustic or mechanical shock wave thereby disrupting the tissue. This mechanism has also sometimes been called photoacoustic, acoustic mechanical, or electromechanical disruption. The most common medical procedure employing this type of tissue effect is posterior capsulotomy to remove the fibrous capsule that sometimes forms secondary to artificial lens implantation for ophthalmology. A Q switch Nd:YAG laser generated peak powers in mega watt range delivered in ultrashort nano second or pica second pulses. The plasma shock wave literally "blows apart" the fibrous capsule. More recently,

exploration in the use of plasmolysis for the disruption of ureteral stones or biliary stones has been investigated with Pulse Dye laser. Pulses of intense light are transmitted through a fiber and directed at calculi through a endoscope. The acousto-mechanical disruption of these calculi yields smaller particles which can be easily excreted. This procedure has been found to yield promising results in treatment for ureteral calculi and biliary calculi.

Photoablation

The process of photoablation is thought to occur through direct breakage of intramolecular bonds. The ultraviolet light is preferentially absorbed by proteins, RNA, and DNA and the wavelength is short enough to allow disruption of these bonds within tissue. The very short pulses also minimize any potential thermal effects and may contribute to the non-thermal cutting. These lasers are known as Excimer lasers and are used in the UvA,B and C wavelengths. Also, because of their very short wavelength, they can be focused into a very small spot size and their depth of penetration is very shallow. Since scattering also is minimized, there is very little effect adjacent to the area of photoablation. Unfortunately, one disadvantage to the use of short wavelengths for photoablation is the possibility of ultraviolet induced mutagenesis.

Thermal Tissue Effects

Hyperthermia

At one step up from photochemistry, and several degrees down from more intense light interaction with tissue is a concept known as hyperthermia. Everyone has felt the warmth of the sun during the summer, and knows the potential of light for heating tissue. If light energy is controlled in its application to tissue in a very slow manner it is possible to heat tissue very gently without causing irreversible damage. The CO_2 laser is difficult to use for this because of its very limited optical penetration depth within tissue. However, the Nd:YAG laser due to its deeper optical penetration depth, may have a heating effect than can be transmitted several millimeters. An experimental treatment of cancer known as hyperthermia takes advantage of the discovery that malignant cells do not tolerate temperatures above 42.5^0 centigrade as well as normal tissues. Therefore, the laser may be used in a low power output to raise tissue temperature within a sphere of tissue significantly enough to effect malignant cell death. The combination of photodynamic therapy with hyperthermia has also been found especially promising. The application of hyperthermia for cancer treatment is not exclusively a demean of lasers, however. Other systems for the generation of heat within tissue include microwaves and magnetic field induction heating which have also been used with similar success to lasers.

Denaturation (welding)

When the tissue temperature is raised above 45 degrees

centigrade, protein de-naturalization may occur. In some cells and tissues this process may be irreversible, but often time results in a slow cell death, and necrosis may not be clinically evident for some time.

Above 60 degrees centigrade, collagen is uncoiled and at higher temperatures is eventually coagulated. Collagen, a triple helix, under mild heating may uncoil and exhibit characteristics of "flowing". Once this has cooled, it may spontaneously re-coil into a helix regaining its basic form. In theory, this de-naturalization/re-naturalization underlies the technique of laser tissue welding. Argon, Nd:YAG and CO_2 lasers have been used in a very small focus, 200 microns, and power densities of 50 to 250 watts per centimeter to weld together skin, nerves, arteries, veins, vas deferens, and bowel. This is accomplished by heating the tissue to a high enough temperature to allow the collagen to flow into itself and then allowing it to cool, thereby binding one edge of the tissue to the other edge. While the tensile strength is low, there is no foreign body reaction involved as there would be if sutures were used, and healing appears to progress in a unimpeded manner.

Coagulation

Between 65 and 70 degrees centigrade, collagen is irreversibly coagulated and cell death is obvious. On microscopic examination with hemotoxin eosin the coagulated zone appears deeply stained with loss of cellulase architecture.

There is a uniformity in appearance across the area of coagulation. Coagulation is the principle means of effecting hemostasis with the laser and the depth or extent of coagulation is directly related to the penetration depth of the laser that is being used. Greatest hemostasis is seen with the Nd:YAG laser and the least hemostasis seen with the Excimer and Erbium:YAG lasers. The potential for hemostasis with the Nd:YAG laser allows the potential for coagulating vessels up to 2 mm in diameter while the CO_2 laser may effectively seal vessels up to 0.5 mm in diameter.

Vaporization

Vaporization of tissue occurs when the water in the tissue is heated above 100 degrees centigrade. At this point, water is converted to vapor and in the conversion to steam ejected from the tissue. Other tissue constituents may also be atomized and injected along with the steam. Ejection velocities of 2 to 3 meters per second have been observed. While the water is vaporized due to the osmotic gradient, fluid is drawn from surrounding tissue and may cause desiccation. This can be seen on the skin where contracture around the impact site may be visualized as ripples or irregularity in the skin surface.

The CO_2 laser since it is absorbed primarily by water is the most efficient at vaporizing tissue, but any laser capable of raising tissue temperature adequately may be used for

vaporization. The total energy applied however, depends upon the ability of tissue to absorb that particular wavelength. For example, while CO_2 is usually absorbed by water, more energy needs to be applied for an Argon or KTP laser to cause tissue vaporization and yet quite a bit more is needed to accomplish the same effect with the Nd:YAG laser.

Tightly focussing a laser beam and drawing it across tissue effectively vaporizes a line of tissue and thus the laser may be used for cutting. If the laser beam is defocused and the power density maintained the same as that for cutting, as the laser is swept over the tissue, ablation of the tissue occurs. This technique is very useful for rapid debulking of large masses.

Carbonization

Biomolecules and constitutes of tissue which are not vaporized or removed with the laser plume may remain in the zone of laser impact. If this material is not effectively heated above its boiling point, it may be reduced to component carbon and remain within the area as a char. Continual application of laser energy to this char may increase the temperature quite beyond 100 degrees centigrade. The potential for reaching temperatures of several thousand degrees centigrade is significant and this mechanism may account for some of the deep thermal effects that are seen around some laser vaporization craters, especially with the carbon dioxide laser. In certain lasers such as the Nd:YAG laser, the char is used as a

chromophore and heat sink. The thermal effect resulting from the absorption of the Nd:YAG laser by this char is actually used to effect tissue thermal coagulation. For CO_2 laser applications especially within the larynx, it is advisable to remove the char during the procedure to minimize the thermal effect deep within the tissue.

Timing of the Laser Pulse

The duration that the laser pulse is in contact with the tissue has important applications for the ultimate tissue effect. As seen from the previous section, long exposures of low power lasers result in photochemical effects, whereas very short exposures of very high powers can result in the formation of a plasma. Between these two extremes, modification of the timing parameters of specific lasers can effect the depth of the thermal effect within tissue. The two most obvious areas that timing plays a critical role is in the use of the Flash Lamp-Excited Dye laser for port wine stains and in the use of CO_2 laser in the suprapulse mode.

The use of the Flash Lamp- Excited Dye laser for decolorization of port wine stains takes advantage of the fact that the wavelength of 577 nanometers is absorbed by hemoglobin very well, resulting in coagulation of the vasculature. However, if the pulse of laser energy is supplied to the tissue for too long, the thermal effect would not only effect the vasculature, but would also have deleterious effects on the tissue surrounding

the vasculature, thus leading to scarring. The Flash Lamp-Excited Eye laser takes advantage of the concepts of thermal diffusion and thermal relaxation time of tissue. Thermal diffusion is the time required for heat to be conducted from the site of energy absorption to an adjacent area, this amount of time is both tissue and area dependent. Thermal relaxation is the time necessary for the tissue to dissipate (^{1}/e of the accumulated heat by re-radiation. This value is independent of area, but is specific for each tissue type. Thermal diffusion times are shorter for highly vascularized tissue, and much longer for bone. The Flash Lamp-Excited Dye laser takes advantage of the vasculature within the port wine stains using a pulse duration of 450 microseconds and an off-time that allows diffusion of the heat away from this area before a second pulse is applied to the tissue. The end result is coagulation only at the vasculature and not the surrounding tissue.

The concept of suprapulse on a CO_2 laser was advanced by Hill in 1967 and given clinical application by Terry Fuller, et al. in 1982. The impact of a CO_2 laser beam on a homogeneous tissue composed of approximately 80% water can visualized, to a first order proximation, as the impact of CO_2 on water. The thermal diffusion for water is 0.001 cm^2/sec and the thermal relaxation time is 0.001 seconds. If the laser pulse is much shorter than the thermal diffusion time, then the heat will not spread beyond the optical penetration depth for that tissue (optical penetration depth is the depth in which light will

penetrate into the tissue with an attenuation of 1/e). If the pulse is then terminated, and a period of time longer than the thermal relaxation time for that tissue is allowed to elapse, the tissue will again return to a steady state base line temperature, thus heat will not accumulate and the thermal effect surrounding the zone of laser vaporization will be minimal. Potential applications include the larynx, where one would wish to limit possible coagulation on the vocalis muscle. The potential for scarring to the underlying vocalis ligament and the associated vibratory mass change for the vocal cord is something one would wish to avoid. Another potential application is in acoustic neuroma dissection close to the 11th nerve where one would wish to limit the thermal spread surrounding the removal of the tumor.

Another method for limiting the duration of the tissue exposure can be accomplished by adjusting the speed of movement the of laser beam across the surface of the tissue. Often, the novice laser surgeon tends to use low power and moves slowly and cautiously which results in longer exposure of the energy to the tissue and deeper thermal coagulation. More experienced surgeons use higher powers with rapid movement. Although total energy delivered is the same in both instances, the expert achieves thermal precision and limited coagulation deep within the tissue.

Clinical Consequences of Tissue Effects

Previous sections have concentrated on demonstrating the initial tissue effects at the cellular level. The clinical consequences of tissue effects may be examined at the tissue and organ system. These include the effects of hemostasis, antisepsis, analgesia, necrosis and the influence on healing.

Hemostasis

The degree of hemostasis available varies between types of lasers and is predictable from the optical penetration depth as discussed earlier. The Neodymium Yag laser which has the deepest optical penetration depth (of 25mm) has the deepest coagulation and can seal blood vessels up to 2mm in diameter with proper application of power parameters. At the other extreme, the CO_2 laser is only able to seal vessels up to 0.5mm in diameter. Even with the carbon dioxide limitations for hemostasis it provides a more bloodless field than a comparable scalpel incision. Several surgeons have elected to use the CO_2 laser for skin incisions. The resultant scar from CO_2 incision at 6 months is almost indistinguishable from a scalpel incision although the early appearance is somewhat disconcerting. CO_2 laser has also been used for mastectomy markedly reducing the blood loss and rate of transfusion for this procedure.

Antisepsis

The thermal effect of laser incision and ablation also and antiseptic property. By raising the tissue temperatures above 100 degrees centigrade. The superficial surface is often sterilized. Bacterial counts of the surface after ablation or

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removal of burn wound eschar with the CO_2 laser have shown marked reduction in bacterial load. In addition, postoperative infection rates have been less following mastectomy performed with the carbon dioxide laser than with scalpel incision.

Analgesia

Several papers have claimed that by use of laser excision or laser incision, the postoperative pain is minimized. The theory behind this is that as the laser cuts or ablates tissue it seals or welds nerve endings closed. This reduces leakage of axoplasm around the end of the cut nerve with decrease in spontaneous deporzation of the nerve. Several studies have claimed this effect, but to date no good prospective controlled studies have been designed to conclusively demonstrate this fact.

Necrosis and Influence on Healing

The depth of necrosis is directly related to the optical penetration depth and thus the coagulation. When tissue temperatures are raised over approximately 45% centigrade, irreversible cell death occurs. Therefore, the magnitude of tissue destruction is greater for those lasers which have deeper optical penetration depth (Nd:YAG is much deeper than CO_2).

The rate of healing depends upon the ability of the body to remove this necrotic tissue. Therefore the rates of healing generally can be expressed linearly going from faster rates of healing for the shallower thermal effect from CO_2 laser to longer rates of healing for KTP and Nd:YAG laser. The scalpel incisions having much less tissue damage on either side of the cut would

heal faster than any of the laser incisions, however when wound tinsel strength is compared at six weeks, there is not difference between scalpel incision and most laser incisions.

Lasers in Otology

Three of the most common medical lasers have all been used at one time or another for various procedures within the ear. The first report of laser use for otology was by Sateloff in using the ruby laser in 1967. This laser was soon abandoned because of poor results. In 1980, Perkins (ref. 1 on Silverstein's paper) reported on laser stapedotomy for otosclerosis using the Argon laser. Since that time, the Argon, KTP and CO_2 lasers have all been used for stapedotomy. In addition, these lasers have been used for tissue welding for tympanoplasty and for vaporization for removal of granulation tissue within the mastoid cavity and middle ear space. It is of note that most people have recognized that the thermal effect from the Nd:YAG laser is too great and have not attempted to apply the Nd:YAG laser for middle ear work or stapedotomies. However, the Nd:YAG has been investigated for heating of the horizontal semi-circular canal in an attempt to control positional vertigo.

Lasers for Tympanoplasty

The three medical lasers have all been used for tympanoplasty. Each laser has been used to try and weld the tympanic membrane into place with moderate success. Most surgeons have not embraced this technique whole-heatedly as the laser

parameters necessary to accomplish the weld are very precise and control is somewhat lacking. However, the use of lasers for removal of granulation tissue in the middle ear space has found application with the use of lasers. Lasers are very effective at tissue vaporization and in this instance, the CO_2 laser is probably the safest laser to use due to its limited thermal penetration depth. One study has looked at the thermal effect of CO_2 laser use over the fallopian canal and concluded that direct application of electromagnetic energy in this region can cause facial paralysis in laboratory animals. The cavity must be extended there for that any radiation or heating over the fallopian canal can be accompanied by facial paralysis and should be avoided.

Lasers for Mastoidectomy

The most common medical lasers have not been used for mastoidectomy except for the removal of granulation tissue encountered within the mastoid. There is not commercially available laser at the present time which is very efficient at removal of bone. The CO_2, KTP and Argon lasers all are done by a similar method. This method involves heating the bone until a char is formed and then picking away at the char. Often times, this char can be removed with minimal effort once the bone has been heated. Concern exists however about the spread of thermal effect around this area of this char. In discussing laser tissue effects, it was noted that when laser energy was continual applied to a char temperatures in access of 2,000 degrees have

been recorded.   Temperatures of this order obviously must be avoided within the ear space.

Lasers Stapedotomy

Many surgeons have promoted the use of the lasers for stapedotomy.   Various proponents have claimed advantages for the CO_2, Argon and the KTP, each for laser stapedotomies.   Reported advantages to the use of the laser include a "non-contact technique", bloodless field, and 3 ease of surgery.

The "non-contact" claim is somewhat misleading however. While the laser is used in a non-contact technique to vaporize the stapes tendon and eventually char the cura and the foot plate, a straight pic must be used to manually remove the char. This involves less pressure than maybe involved with drilling out the foot plate with a rotating burr or a buckingham hand drill but is not a true "non-contact technique".

Each laser has unique advantages and disadvantages in regard to stapedotomy.   The Argon and KTP lasers are not absorbed by white bone and therefore, much of the energy is reflected from the surface of the foot plate until the heat has caused a char formation then the laser is absorbed quite adequately at the foot plate site.   Potential difficulties with both the use of the Argon and by extension, the KTP laser include energy transmission through an intact foot plate.   Several authors have demonstrated temperature rises within the vestibule after application of Argon and KTP laser to an intact stapes foot plate.   In addition, Boraf in studying stapedotomies performed with an Argon laser on cats

noted damage to the sacculi on 3 of 8 cats. This damage was due
to the beam transmitting across the clear fluid and impacting on
the sacculi directly opposite the stapedotomy site. While this
has not been documented with KTP laser, the visible wavelength of
KTP being so close to that of Argon this possibility must be
considered as well. The CO_2 laser does not vaporize bone per
say. It also works by creating a char on the foot plate which
must be then picked away using a straight pic. The CO_2 laser
having a small thermal damage radius and very high absorption by
water is then rapidly absorbed by the surface of the perilymph.
While some surgeons have cautioned about the possibility of
boiling the surface of the perilymph Lesinski has shown that the
temperature rise with the perilymph is limited to 1 degrees
centigrade or less and can be modified by appropriate selection
of pulse parameters with the CO_2 laser.

Overall results for the use of the laser to perform
stapedotomies have delivered results comparable and in some cases
slightly superior to results obtained by conventional techniques
using rotating burr or buckingham hand drill. Silverstein's most
recent reporting better overall hearing results when compared to
conventional techniques also noted an increase incidence in
postop vertigo with the use of the KTP laser. He stated that all
vertigo had responded within 3 weeks however.

Conclusion

The use of lasers for otologic surgery has been performed
safely through judicious use of pulse parameters to limit thermal

effect. Overall, results are comparable to conventional
techniques and in some hands may actually be superior. The
extensive thermal effect from use of Argon and KTP lasers must be
considered and the anatomy fully appreciated before application
of energy from these two units is employed. The CO_2 laser while
having less thermal effect is still not without draw-backs. The
ultimate answer of which laser to use and when in ear surgery has
not yet been determined.

References

1.   Marhic M: The free-electron laser: A powerful source of broadly tunable coherent radiation. Bio-Laser News 1985; 1-3.

2.   Einstein A: Zur quantentheorie der strahlung. Physik Zeitschr 1917; 17:121-128.

3.   Apfelberg DB: Biophysics, advantages, and installation of laser systems, in Apfelberg DB (ed): Evaluation and Installation of Surgical Laser Systems. New York, Springer-Verlag, 1987, pp 1-17.

4.   Fuller TA: Fundamentals of lasers in surgery and medicine, in Dixon JA (ed): Surgical Applications of Lasers. Chicago, New Book Medical Publishers, Inc, 1983, pp 11-28.

5.   Goldman L: Comparison of the biomedical effects of the exposure of human tissues to low and high energy lasers. Ann NY Acad Sci 1965; 122:802-813.

6.   Jako GJ: Laser surgery of the vocal cords. Laryngoscope 1972; 82:2204-2216.

7.   Sataloff J: Experimental use of laser in otosclerotic stapes. Arch Otolaryngol 1967; 85:58-60.

8.   Council on Scientific Affairs: Lasers in medicine and surgery. JAMA 1986; 256:900-907.

9.   Fuller TA: The physics of surgical lasers. Lasers Surg Med 1980; 1:5-14.

10. Polanyi TG: Physics of surgery with lasers. Clin Chest Med 1985; 6:179-202.

11. Stein BS: Laser physics and tissue interaction. Urol Clin North Am 1986; 13:365-380.

12. Fuller TA: Fundamentals of laser surgery, in Fuller TA (ed): Surgical Lasers. New York, Macmillan Publishing Co, Inc, 1987, pp 1-17.

13. Stamp JM: An introduction to medical lasers. Clin Phys Physiol Meas 1983; 4:267-290.

14. Boulnois JL: Photophysical processes in recent medical laser developments: A review. Lasers Med Sci 1986; 1:47-66.

15. Mainster, MA: Finding your way in the photoforest: Laser effects for clinicians. Ophthalmology 1984: 91-886-888.

16. Sliney DH: Laser-tissue interactions. Clin Chest Med 1985; 6:203-208.

17. Haldorsson T, Langerhold J: Thermodynamic analysis of laser irradiation of biological tissue. Appl Optics 1978; 17:3948-3958.

18. Polanyi TG, Bredemeir HC, Davis TW: A CO_2 laser for surgical research. Med Biol Eng 1970; 8:541-548.

19. Deckelbaum LI, Isner JM, Donaldson RF, et al: Reduction of laser-induced pathologic tissue injury using pulsed energy delivery. Am J Cardiol 1985; 56:662-667.

20. Hill AJ: Multijoule pulses from CO_2 lasers. Appl Phys Lett 1968; 12:324-327.

21. Walsh JT, Flotte TJ, Anderson RR, et al: Pulsed CO_2 laser tissue ablation: Effect of tissue type and pulse duration on thermal damage. Lasers Surg Med 1988; 8:108-118.

22. Hobbs ER, Baililn PP, Wheeland RG, et al: Superpulsed lasers: Minimizing thermal damage with short duration, high irradiance pulses. J Dermatol Surg Oncol 1987; 13:955-964.

23. Rattner WH, Rosemberg SK, Fuller T: Difference between continous wave and superpulse carbon dioxide laser in bladder surgery. Urology 1979; 13:264-266.

24. Lanzafame RJ, Naim JO, Rodgers DW, et al: Comparison of continuous-wave, chop-wave, and super pulse laser wounds. Lasers Surg Med 1988; 8;119-124.

25. McKenzie AL, Carruth JAS: Lasers in surgery and medicine. Phys Med Biol 1984; 29:619-641.

26. Ossoff RH, Duncavage JA: Past, present, and future usage of lasers in otolaryngology-head and neck surgery, in Aptelberg DB (ed): Evaluation and Installation of Surgical Laser Systems. New York, Springer-Verlag NY, 1987; pp 127-149.

27. Norris CW, Mullarky MB: Experimental skin incision made with the carbon dioxide laser. Laryngoscope 1982; 92:416-419.

28. DiBartolomeo JR: The argon and CO_2 lasers in otolaryngology: Which one, when and why? Laryngoscope 1981; 91: 1-16.

29.   Report of Panel on Lasers in Medicine and Surgery, Part I.
      Conn Med 1986; 50:406-409.

30.   Morelli JG, Tan OT, Garden J, et al: Tunable dye laser (577
      nm) treatment of port wine stains. Lasers Surg Med 1986;
      6:94-99.

31.   Report of Panel on Laser in Medicine and Surgery, Part II.
      Conn Med 1986; 50:466-470.

32.   Isner JM, Donaldson RJ, Decklebaum LI, et al: The excimer
      laser: Gross, light microscopic and ultrastructural
      analysis of potential advantages for use in laser therapy
      of cardiovascular disease. J Am Coll Cardiol 1985; 6:1102-
      1109.

33.   Medical application of the excimer laser. Lancet 1986;
      2:82-83.

34.   Fuller TA, Nadkarni VJ, Pavlov IK, et al: Carbon dioxide
      laser fiber optics. Bio-Laser News 1985; April: 1-6.

35.   Fuller TA: Mid-infared fiber optics. Lasers Surg Med 1986;
      6:399-403.

36.   Weiss R: Advances in infared fibers. Laser Optronics 1988:
      7:29-37.

37.   Stone J, Earl HE, Derosier RM: Measurement set for optical
      fiber loss spectra., Rev Sci Instrum 1982; 53:197-201.

38.   Mehta AC, Livingston DR, Golish JA: Artificial sapphire
      contact endoprobe with Nd-YAG laser in the treatment of
      subglottic stenosis. Chest 1987; 91:473-474.

39. Shapshay SM: Laser application in the trachea and bronchi: A comparative study of the soft tissue effects using contant and non-contact delivery systems. Laryngoscope 1987; 97(suppl 41):1-26.

40. Baggish MS, ElBakry MM: A flexible CO_2 laser fiber for operative laparoscopy. Fertil Steril 1986: 46:16-20.

41. Beckman H, Fuller TA: Carbon dioxide laser fiber optics in endoscopy, in Atsumi K (ed): New Frontiers in Laser Medicine and Surgery. Amsterdam, Excerpta Medica 1983, pp 76-80.

42. Ossoff RH: Bronchoscopic laser surgery: Which laser when and why. Otolaryngol Head Neck Surg 1986; 94:378-381.

43. Fried MP: Complications of CO_2 laser surgery of the larynx. Laryngoscope 1983; 93:275-278.

44. Fava G, Emanuelli H, Cascinelli N, et al: CO_2 lasers: Beam patterns in relation to surgical use. Lasers Surg Med 1983; 2:331-341.

45. Bodecker V, Buchholz J, Drake KH, et al: Influence of thermal effects on the width of necrotic zones during cutting and coagulating with laser beams. Presented at the Second International Symposium on Laser Surgery. Dallas, October 23-26, 1977, pp 101-108.

46. Burke L, Rovin RA, Cerullo LJ, et al: Thermal effects of the Nd:YAG and carbon dioxide lasers on the central nervous system. Lasers Surg Med 1985; 5:67-71.

47. Anderson RR, Hu J, Parrish JA: Optical radiation transfer in the human skin and application in vivo remittance spectroscopy, in Marks R, Payne PA (eds): Bioengineering and the Skin. Lancaster, England, MTP Press Limited, 1979, pp 253-265.

48. Anderson RR, Parrish JA: The optics of human skin, J Invest Dermatol 1981; 77:13-19.

49. Bruls WAG, van der Leun JC: Forward scattering properties of human epidermal layers. Photochem Photobiol 1984; 40:231-242.

50. Solon LR, Sims SD: Fundamental physiological optics of laser beams. Med Res Eng 1970; 9:10-25.

51. Evans LR, Sims SD: Fundamental physiological optics of laser beams in biomedical studies. Phy Med Biol 1969; 14:205-212.

52. Kolari PJ: Penetration of unfocused laser light into the skin. Arch Dermatol Res 1985; 277:342-344.

53. Pratessi R, Ronchi L, Cecchi G, et al: Skin optics and phototherapy of jaundice. Photochem Photobiol 1984; 40:77-83.

54. Wan S, Parrish JA, Anderson RR, et al: Transmittance of nonionizing radiation in human tissues. Photochem Photobiol 1981; 34:679-681.

55. Ertefai S, Profiio AE: Spectral transmittance and contrast in breast diaphanography. Med Phys 1985; 12:393-400.

56.   Profio AE, Doiron DR: Dosimetry considerations in
      phototherapy. Med Phys 1981; 8:190-196.

57.   Werkhaven JA, Harris DM, Krol G, et al: Light dosimetry in
      animal models, application to photodynamic therapy in
      otolaryngology. Laryngoscope 1986; 96:1058-1061.

58.   Harris DM, Hill JH, Werkhaven JA, et al: Prophyrin
      flourescence and photosensitization in head and neck
      cancer. Arch Otolaryngol Head and Neck Surg 1986; 112:1194-
      1199.

59.   Harris DM, Werkhaven JA: Endogenous porphyrin flourescence
      in tumors. Lasers Surg Med 1987; 7:467-472.

60.   Bayly JG, Kartha VB, Stevens WH: The absorption spectra of
      liquid phase H_2O and D_2O from .7 mm to 10 mm. Infrared Phys
      1963; 3:211-222.

61.   Wolbarsht ML: Laser Surgery: CO_2 or HF. IEEE J Quantum
      Electronics 1984;20:1427-1432.

62.   Smith T, Apfelberg DB, Maser MR, et al: 532-nanometer green
      laser beam treatment of superficial varicosities of the
      lower extremities. Laser Surg Med 1988; 8:130-134.

63.   Apfelberg DB, Maser MR, Lash H, et al: The role of the
      argonlaser inteh management of hemangiomas. In J Dermatol
      1982; 21:579-589.

64.   Apfelberg DB, Bailin P, Rosenberg H: Preliminary
      investigation of KTP/532 laser light in the treatment of
      hemangiomas and tattoos. Laser Surg Med 1986; 6:38-42.

65. Lahaye CTW, Van Gemert MJC: Optimal laser parameters for port wine stain therapy: A theoretical approach. Phys Med Biol 1985; 30:573-576.

66. Greenwald J, Rosen S, Anderson RR, et al: Comparative histological studies of the tunable dye (at 577 nm) laser and argon laser: The specific vascular effects of the dye laser. J Invest Dermatol 1981; 77:305-310.

67. Hulsbergen JP, Van Gemert MJC: Port wine stain coagulation experiments with a 540 nm continuous wave dye-laser. Lasers Surg Med 1983; 2:205-210.

68. Landthaler M, Haina D, Brunner R, et al: Effects of argon, dye and Nd:YAG lasers on epidermis, dermis, and venous vessels. Lasers Surg Med 1986; 6:87-93.

69. Dougherty TJ, Kaufman JE, Goldfarb A, et al: Photoradiation therapy for the treatment of malignant tumors. Cancer Res 1978; 38:2628-2635.

70. Karu TI: Photobiological fundamentals of low-power laser therapy. IEEE J Quantum Electronics 1987; 23:1703-1717.

71. Gomer CJ, Dougherty TJ: Determination of $[^3H]$- and $[^{14}C]$ hematoporphyrin derivative distribution in malignant and normal tissue. Cancer Res 1979; 39:146-151.

72. Kessel D: Determinants of hematoporphyrin-catalyzed photosensitization. Photochem Photobiol 1982; 36:99-101.

73. Weishaupt KR, Gomer CJ, Dougherty TJ: Identification of singlet oxygen as the cytoxic agent in photo-inactivation of a murine tumor. Cancer Res 1976; 36:2326-2329.

74. McCaughjan JS, Guy JT, Hawley P, et al: Hematoporphyrin-derivative and photoradiation therapy of malignant tumors. Lasers Surg Med 1983; 3:199-209.

75. Moan J: Porphyrin-sensitized photodynamic inactivation of cells: A review. Lasers Med Sci 1986; 1:5-12.

76. Wile AG, Novotny J, Mason GR, et al: Photoradiation therapy of head and neck cancer. Am J Clin Oncol 1984; 6:39-43.

77. Harris DM: Establishing the scientific basis of laser biostimulation. LIA Laser Top 1988; 10:9-14.

78. Dretler SP: Review: Laser lithotripsy. A review of 20 years of research and clinical applications. Lasers Surg Med f19898; 8:341-356.

79. Medical application of the excimer laser. Lancet 1986; 2:82-83.

80. Parrish JA: Ultraviolet-laser ablation. Arch Dermatol 1985; 121:599-600.

81. Svaasand LO, Boerslid T, Oeveraasen M: Thermal and optical properties of living tissue: Application to laser-induced hyperthermia. Lasers Surg Med 1985; 12:455-461.

82. Svaasand LO: Photodynamic and photohyperthermic response of malignant tumors. Med Phys 1985; 12:455-461.

83. Daikuzono N, Suzuki S, Tajiri H, et al: Laserthermia: A new computer-controlled contact ND:YAG system for interstitial local hyperthermia. Lasers Surg Med 1988; 8:254-461.

84. Quigley MR, Bailes JE, Kwaan HC, et al: Microvascular anastomosis using the milliwatt CO_2 laser. Lasers Surg Med 1985; 12:455-461.

85. Ulrich R, Durselen R, Schober R: Long-term investigations of laser-assisted microvascular anastomoses with the 1.318-mm ND:YAG laser. Lasers Surg Med 1988; 8:104-107.

86. Ashworth EM, Dalsing MC, Olson JF, et al: Large artery welding with a miliwatt carbon dioxide laser. Arch Surg 1987; 122:673-677.

87. Garden JM, Robinson JK, Taute PM, et al: The low-output carbon dioxide laser for cutaneous wound closure of scalpel incisions: Comparative tensile strength studies of the laser to the suture and staple for wound closure. Lasers Surg Med 1986; 6:67-71.

88. White RA, Abergel RP, Klein SR, et al: Laser welding of venotomies. Arch Surg 1986; 121:905-907.

89. Anderson RR, Jaenicke KF, Parrish JA: Mechanisms of selective vascular changes caused by dye lasers. Lasers Surg Med 1983; 3:211-215.

90. Mihashi S, Jako GJ, Incze J, et al: Laser surgery in otolaryngology: Interaction of CO_2 laser and soft tissue. Ann NY Acad Sci 1976; 267:263-293.

91. Komisar A, Ruben RJ: Use of the carbon dioxide laser in pediatric otolaryngologic disease. NY State J Med 1981; 81:1761-1764.

92.   Meyers AD, Kuzela DC: Dose-response characteristics of the
       human larynx with carbon dioxide laser radiation. Am J
       Otolaryngol 1980; 1:136-140.

93.   Werkhaven JA, Harris DM: Superpulse CO_2 laser tissue
       effects. Presented at the Second International Laser
       Surgery Congress, Nashville, Tenn, June 22-24, 1988.

94.   Bellina JH, Meandzija MP, Shillt V, et al: Analysis of
       electronically pulsed versus quasi-continuous wave carbon
       dioxide lasers in an animal model. Am J Obstet Gynecol
       1984; 150: 934-940.

95.   Baggish MS, ElBakry MM: Comparison of electronically
       superpulsed and continuous-wave CO_2 laser on the rat
       uterine horn. Fertil Steril 1986; 45:120-127.

96.   Sinofsky E: Comparative thermal modeling of Er:YAG, Ho:YAG,
       and CO_2 laser pulses for tissue vaporization. Proceedings
       of SPIE. Laser Med 1986; 712:188-192.

97.   Armon E, Laufer G: Asymptotic and dimensionless analysis of
       the response of living tissue to surgical pulsed CO_2
       lasers. Biomechanical Engineering 1986; 108:368-371.

98.   Apfelberg DB, Maser MR, Lash H, et al: Benefits of the CO_2
       laser in oral hemangioma excision. Plast Reconstr Surg
       1985; 75:46-50.

99.   Apfelberg DB, Maser MR, Lash H: Review of usage of argon
       and carbon dioxide lasers for pediatric hemangiomas. Ann
       Plast Surg 1985; 75:46-50.

100. Carruth JAS, Shakespeare P: Toward the ideal treatment for the port wine stain with the argon laser: Better prediction and "optimal" technique. Lasers Surg Med 1986; 6:2-4.

101. Hobby LW: Argon laser treatment of superficial vascular lesions in children. Lasers Surg Med 1986; 6:16-19.

102. Hulsbergen JP, Van Gemert MJC, Lahaye CTW: Clinical and histological evaluation of port wine stain treatment with a microsecond-pulsed dye-laser at 577nm. Lasers Surg Med 1984; 4:375-380.

103. Levine NS, Salisbury RE, Peterson HD, et al: Clinical evaluation of the carbon dioxide laser for burn wound excisions: A comparison of the laser scalpel, and electrocautery. J Trauma 1975; 15:800-807.

104. Lanzafame RJ, Rodgers DW, Naim JO, et al: The effect of the CO_2 laser excision on local tumor recurrence. Lasers Surg Med 1986; 6:103-105.

105. Madden JE, Edlich RF, Custer JR, et al: Studies in the management of the contaminated wound, IV. Resistance to infection of surgical wounds made by knife, electrosurgery, and laser. Am J Surg 1970; 119:222-224.

106. Allan SN, Spitz L, Van Noort R, et al: A comparative study of scalpel and electrosurgical incision on subsequent wound healing. J Pediatr Surg 1982; 17:52-54.

107. Bellina JH, Hemmings R, Voros JI, et al: Carbon dioxide
      laser and electrosurgical wound study with an animal
      model: A comparison of tissue damage and healing patterns
      in peritoneal tissue. Am J Obstet Gynecol 1984; 148:327-
      334.

108. Buell BR, Schuller DE: Comparison of tensile strength in
      CO_2 laser and scalpel skin incisions. Arch Otolaryngol
      1983; 109:465-467.

109. Schroder T, Joffe N: Will lasers replace electrocautery in
      surgery? Ann Chir Gynaecol 1986; 75:3-4.

110. Lesinski GS, Palmer A: Lasers for Otosclerosis: CO_2 vs.
      Argon and KTP-532. Laryngoscope; 1989, 99:1-12.

111. Lesinski SK, Stein JA: Stapedectomy Revision with the CO_2
      Laser. Laryngoscope, 1989, 99:(Suppl. 46):13-24.

112. Lesinski SG, Palmer A: CO_2 laser for otosclerosis: Safe
      energy parameters. Laryngoscope, 1989, 99:9-12.

113. Lensinski SG, Stein JA: CO_2 laser stapedectomy.
      Laryngoscope, 1989, 99:20-24.

114. Silverstein H, Rosenberg S, Jones R: Small fenestra
      stapedotomies with and without KTP laser: A comparison.
      Laryngoscope, 1989 99:485-488.

115. Perkins RC: Laser stapedectomy for Otosclerosis.
      Laryngoscope, 1980, 90:228-241.

116. Gantz BJ, Jenkins HA, Kishimoto S., et al: Argon laser
      stapedectomy. Ann Otol, 1982, 92:25-26.

117. Vollrath V, Schreiner M: Influence of argon laser stapedectomy on cochlear potentials. Acta Otolaryngol, (Stockh), Suppl, 1982, 385:1-32.

118. Vollrath M, Schreiner M: The effects of the argon laser on temperature within the cochlea. Acta Otolaryngol (Stockh), 1982, 93:341-348.

119. Ricci T, Mazzoni M: Experimental investigation of temperature gradients in the inner ear following argon laser exposure. J Laryngol Otol, 1985, 99:359-362.

120. McGee TM: The argon laser in surgery for chronic ear disease and otosclerosis. Laryngoscope, 1983, 93:1177-1182.

121. DiBartolomeo JR, Ellis M: The argon laser in otology. Laryngoscope, 1980, 90:1786-1796.

122. Vollrath M, Schreiner C: The effects of the argon laser on temperature within the cochlea. Acta Otolaryngol, 1981, 93:341-348.

123. Ator GA, Coker NJ, Jenkins HA: Thermal injury to the infratemporal facial nerve following CO_2 laser application. Am J of Otolaryngol, 1985, 437-442.

124. Thomas J, Unger V, Kastenbauer E: Temperature-und Druckmessungen im Innenohr bei der Anwendung des Argon-Laser. Laryngol Rhinol, 1981, 60:587-590.

125. Sataloff J: Experimental use of laser in otosclerosis stapes. Arch Otolaryngol, 1967, 85:58-60.

126. McGhee TM: The argon laser in surgery for chronic ear disease and otosclerosis. Laryngoscope, 1983, 93:1177-1181.

127. Myer CM, Miller GW, Keith RW: Use of the neodymium/yttrium aluminum garnet laser in middle ear surgery: A preliminary report. Am J of Otolaryngol, 1986, 7:38-40.

128. Coker NJ, Ator GA, Jenkins HA, Neblett CR, Morris JR: Carbon dioxide laser stapedectomy. Arch Otolaryngol, 1985, 3:601-605.

129. Coker NJ, Ator GA, Jenkins HA, Neblett CR: Carbon Dioxide laser stapedotomy: A histopathologic study. Am Jour of Otolaryngol, 1986, 7:253-257.

130. Epley JM: Tympanic membrane debridement with the CO_2 laser. Otolaryngol Head Neck Surg, 1981, 89:898-902.

131. Escudero LH, Castro AO, Drumond M, Porto S, Bozinis DG, Penna FS, Gallego-Liuesma E: Argon Laser in Human Tympanoplasty. Arch Otolaryngol, 1979, 105:252-253.

132. Garner G, Robertson JH, Tomoda K, Clark WC: CO_2 Laser stapedectomy: Is it practical?, Am J Otolaryngol, 1984, 5:108-117.

133. Goode RL: CO_2 laser myringotomy. Laryngoscope, 1982, 92:420-423.